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PREVALENCE OF TOXOPLASMOSIS AND ITS ASSOCIATION WITH DEMENTIA IN OLDER ADULTS IN CENTRAL AFRICA: A RESULT FROM THE EPIDEMCA PROGRAMME

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Abstract:	Objective: This study aimed at estimating the seroprevalence of Toxoplasma gondii infection in older adults living in Central Africa and at investigating its association with dementia using data from the Epidemiology of Dementia in Central Africa programme, a population-based study. Methods: A cross-sectional multicenter population-based study was carried out among participants aged ≥65 years living in rural and urban areas of the Central African Republic and the Republic of Congo. Blood samples were collected from each consenting participant. The detection of anti-T.gondii immunoglobulin G antibodies was done in France using a commercially available ELISA kit. Participants were interviewed using a standardized questionnaire including sociodemographic characteristics. DSM-IV criteria were required for a diagnosis of dementia. Multivariate binary logistic regression models were used to estimate the association between toxoplasmosis infection and dementia. Results: Among 1,662 participants, the seroprevalence of toxoplasmosis was 63.0% (95% confidence interval (CI): 60.7-65.3) overall, 66.6% (95%CI: 63.4-69.8) in Central African Republic and 59.4% (95%CI: 56.1-62.7) in the Republic of Congo. In multivariate analyses, toxoplasmosis status was significantly associated with

	increasing age (p=0.006), Republic of Congo (p=0.002), urban area (p=0.001) and previous occupation (p=0.002). No associations between dementia and toxoplasmosis status or anti- T gondii IgG titres were found. Conclusion: Being infected with T. gondii was not associated with dementia among older adults in Central Africa. Our findings are consistent with some previous studies and add to the knowledge on the relationship between T. gondii infection and neurological disorders.

PREVALENCE OF TOXOPLASMOSIS AND ITS ASSOCIATION WITH DEMENTIA IN OLDER ADULTS IN CENTRAL AFRICA: A RESULT FROM THE EPIDEMCA PROGRAMME

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Running title: Toxoplasmosis and dementia in Central

ABSTRACT (241 words)

Objective: We aimed at estimating the seroprevalence of *Toxoplasma gondii* infection in older adults living in Central Africa and investigating its association with dementia using data from the Epidemiology of Dementia in Central Africa (EPIDEMCA) programme.

Methods: A cross-sectional multicentre population-based study was carried out among participants aged 73 (±7) years on average, living in rural and urban areas of the Central African Republic and the Republic of Congo between November 2011 and December 2012. Blood samples were collected from each consenting participant. The detection of anti-*T.gondii* immunoglobulin G antibodies was performed in 2014 in France using a commercially available ELISA kit. Participants were interviewed using a standardized questionnaire including sociodemographic characteristics. DSM-IV criteria were required for a diagnosis of dementia. Multivariate binary logistic regression models were used to estimate the association between toxoplasmosis infection and dementia.

Results: Among 1,662 participants, the seroprevalence of toxoplasmosis was 63.0% (95% confidence interval (CI): 60.7-65.3) overall, 66.6% (95%CI: 63.4-69.8) in Central African Republic and 59.4% (95%CI: 56.1-62.7) in the Republic of Congo. In multivariate analyses, toxoplasmosis status was significantly associated with increasing age (p=0.006), Republic of Congo (p=0.002), urban area (p=0.001) and previous occupation (p=0.002). No associations between dementia and toxoplasmosis status or anti- *T.gondii* IgG titres were found.

Conclusion: *T.gondii* infection was not associated with dementia among older adults in Central Africa. Our findings are consistent with previous studies and add to the knowledge on the relationship between *T.gondii* infection and neurological disorders.

Keywords: Dementia, Alzheimer's Disease, *Toxoplasma gondii*, seroprevalence, older adults, sub-Saharan Africa

INTRODUCTION (3,103 words)

Globally, 25-30% of individuals are infected with *Toxoplasma gondii* (*T.gondii*) (1;2) with disparities across regions, depending on geographical and socio-economic conditions (1;2). Previous studies estimated at around 40% the prevalence of *T.gondii* infection in general population in the Republic of Congo (ROC) and in the Central African Republic (CAR) (3;4;4). *T.gondii* infection seroprevalence is primarily studied in population at risk for developing acute toxoplasmosis such as women of childbearing age and immuno-compromised patients. Although the risk of being infected with *T.gondii* increases with age (5), its prevalence among older adults and the effect of age on anti-*T.gondii* antibody titre evolution remain largely unknown.

During a primary *T.gondii* infection, the invasive tachyzoite stages circulate in the blood, invade the various organs, cross the blood-brain barrier and establish themselves in the brain cells probably as soon as the end of the first week of infection. This acute toxoplasmosis phase lasts a few weeks. It is usually asymptomatic, but can also present as a benign disease with lymphadenopathies, fever and asthenia. Beyond this acute phase, the invasive tachyzoite stages are no longer present, and the chronic stage of infection is characterized by the presence of latent toxoplasmic cysts in the tissues, and more particularly the central nervous system. This chronic stage is assumed to persist throughout life without inducing any symptoms in immunocompetent patients (1).

Dementia is a neurodegenerative disease characterized by progressive decline in cognitive functions, progressive functional impairment, and behavioural and psychological symptoms (6). Alzheimer's disease, characterized by two core cerebral lesions (β amyloid plaques and neurofibrillary tangles), is the most common cause of dementia among older people. Lewy Body disease, frontotemporal lobar degeneration, and vascular disease, are other common causes of dementia, differing in pathophysiology (7). However, mixed pathologies are much more common than 'pure' forms of dementia (8). Dementia has a significant impact on those affected, their families and society, with considerable costs worldwide (9). Demographic ageing worldwide is expected to lead to a dramatic increase in the number of cases, and African countries are not spared by this phenomenon (10). The

prevalence of dementia in adults aged 65 years and older was recently estimated between 6.4% and 8.5% in CAR and between 5.7% and 6.7% in ROC (11;12).

Literature studying the association between latent *T.gondii* infection and neurological or psychiatric disorders is growing (13-17). Chronic infection compromised goal-directed behaviour (18), affected several aspects of memory (19;20), led to a decline in visual motor coordination, coding ability and short term memory (21), and to a more rapid decline in executive function and cognitive decline among older adults (21). Cognitive dysfunctions were attributed to cysts' location in the brain (22;23), to the immune response in chronically infected patients (24), or to a change in cerebral metabolism (23;25). A chronic infection accompanied by an increase in interferon γ (IFN-γ) production decreases the tryptophan pool affecting kynurenic acid and serotonin levels. Moreover, *T.gondii* infection increases the activity of the tyrosine hydrolase that in turn releases dopamine. The increase in kynurenic acid and dopamine levels along with the decrease in serotonin level were associated with cognitive dysfunctions in rodents (23;26;27) and in humans (28). *T.gondii* infection was however shown to decrease β-amyloid plaque deposition in the cortex and hippocampus suggesting positive effects of *T.gondii* infection on the pathogenesis and progression of Alzheimer's disease (AD) in mice (29-31). In humans, case-control studies dedicated to *T.gondii* infection and dementia reported contradictory results (32-35). Most studies focused on the Alzheimer's subtype (32;33;35). Two studies found no association between AD and toxoplamosis infection in the USA (33) and in Iran (32) whilst the third one in Turkey suggested that toxoplasma infection may be involved in the pathogenetic mechanisms of AD (35). The only study investigating dementia (all subtypes combined), in Egypt, showed that toxoplasma positive participants had an increased likelihood of having dementia, regardless of their ApoE genotype (34). To our knowledge, no study has been conducted in sub-Saharan African countries yet, where both dementia and *T. gondii* epidemiology may present particular aspects.

We aimed first at estimating the seroprevalence of *T.gondii* infection among older adults in Central Africa; secondly, at investigating the association between *T.gondii* infection and dementia, within the

Epidemiology of Dementia in Central Africa (EPIDEMCA) programme, a large population-based study.

METHODS

Participants

Our study population consisted of participants included in the EPIDEMCA programme, a multicentre cross-sectional population-based study conducted in CAR and ROC between November 2011 and December 2012. The detailed methodology is described in an open access publication (36). In essence, participants aged 65 years and older who had lived in the study area for at least six months were included. The study areas included the capitals of CAR (Bangui) and ROC (Brazzaville), and two rural areas (Nola in CAR and Gamboma in ROC). The sample size was calculated *a priori* with the aim of estimating dementia prevalence, and was then rounded at 500 in each study site. In absence of detailed census, the participants' selection in urban areas was carried out using a proportional random sampling (to represent Bangui and Brazzaville's diverse populations) while a door-to-door approach was preferred due to logistic and financial constraints in rural areas. Response rates varied between 93 and 97% across sites, with the only exclusion criteria being refusal or the presence of severe disease with short-term high risk of death.

Approvals were obtained from the ethical committee supervised by the Ministry of Public Health in CAR, the Comité d'Éthique de la Recherche en Sciences de Santé in ROC, and an ethical review board from the Comité de Protection des Personnes du Sud-Ouest et d'Outre-Mer 4 in France. All participants and/or their families gave informed consent prior to inclusion in the study. Written consent was obtained when feasible. Consent was obtained by thumbprint for illiterate people.

Serological analysis

Each consenting participant had 20 mL of blood collected into two polypropylene EDTA tubes by a dedicated nurse. Whole fresh blood samples were centrifuged and aliquoted within few hours to avoid degradation due to high temperatures and then frozen at -20°C or -80°C in the nearest laboratory. Plasma aliquots were stored at the Pasteur Institute of Bangui in CAR and the National Laboratory of

Public Health in Brazzaville in ROC before dry-ice shipping to the University of Limoges where plasma samples were kept stored at -80°C until analysed. In 2014, the detection of anti-*T.gondii* immunoglobulin G (IgG) was done using the VIDAS TOXO IgG II test (Biomérieux, France), according to the manufacturer's instructions. This test is validated for detection of anti-*T.gondii* IgG in plasma. Results were reported in International Units per millilitre (IU/mL). Samples with anti-*T.gondii* IgG <4 IU/mL were considered as seronegative. A sample was considered as positive when the titre was equal or greater than 8 IU/mL. Samples with titres ≥300 UI/mL were diluted in the negative control included with the VIDAS TOXO IgG II test until titres could be determined. Titres comprised between 4 IU/mL and 8 IU/mL were considered as equivocal and further analysed by VIDAS TOXO competition (Biomérieux, France), which better correlated with low titres of the usual reference test, namely dye-test. Samples with indexes below 1.6 were considered as seropositive according to the manufacturer's instructions. The *T.gondii* positive group included all participants that were positive either with VIDAS Toxo IgG II or with VIDAS Toxo Competition assay.

Dementia assessment

Dementia was assessed following a two-stage process. First, cognitive screening was performed using the Community Screening Interview for Dementia (CSI-D) (37) adapted, back-translated and pretested in the local languages (Sango in CAR, Lari, Lingala, and Kituba in ROC). Every participant obtaining a poor performance on the CSI-D cognitive tests (COGSCORE ≤24.5) was suspected of having cognitive impairment and referred for neurological assessment. During the second phase which was conducted at the hospital 3-14 weeks later, further psychometric tests were conducted, including the Free and Cued Selective Reminding Test (38), Zazzo's cancellation task (39) and Isaac's Set Test of verbal fluency (40). Neurologists performed clinical examination, recorded history of stroke and presence of depressive disorders, and assessed orientation skills and daily activities. Dementia was diagnosed according to the DSM-IV criteria (6). An experienced neurologist (JFD) reviewed all medical records and cognitive test performances in order to reach a consensus.

Statistical analysis

Sociodemographic data included age, sex, marital status (married, never married/widowed/divorced/separated), education (no education, at least primary school), occupation (farmer/breeder/fisher *vs*. other), country (CAR, ROC) and area (urban, rural). Age was ascertained from official documents, using historical events or from an informant if previous methods were unsuccessful. All variables were collected during the first phase in all participants.

Study population characteristics were described in terms of means with corresponding standard deviations for age, median with its inter-quartiles range (IQR) for antibody titres and cognitive scores, and percentages for all categorical variables. Prevalence of toxoplasmosis was presented with its 95% confidence interval (CI). Comparisons were carried out between countries using the Chi-square test and Kruskal-Wallis test when appropriate. The correlation between the anti-IgG titre and age was tested using the Spearman test.

Factors associated with *T.gondii* infection were examined using logistic regression models. All factors associated with *T.gondii* infection and dementia at $p<0.20$ in univariate analysis were included in multivariate logistic regression model. The variable selection was carried out using a backward stepwise approach in which variables considered to be a confounder (odds ratio's variation above 15%) were kept in the model. The association between toxoplasmosis and dementia was first analysed in unadjusted logistic regression model and then in a model adjusted for age, sex, country, area and education.

In a sensitivity analysis, we ran the fully-adjusted logistic regression model with quintiles of anti-IgG titres as dependent variable instead of toxoplasmosis status.

The level of significance was fixed at 0.05 for all analyses. Statistical analyses were carried-out using Stata version 10.1 for Windows (StataCorp, College Station, TX).

RESULTS

Characteristics of the EPIDEMCA participants

Among 2,002 participants included in the EPIDEMCA study, 340 participants were excluded because they did not have blood samples due to refusals (n=176), impossible blood withdrawal (n=35), poor

health conditions (n=34), absence on the day of blood collections (n=9), and non-exploitable samples (n=86). A total of 1,662 participants were therefore analysed (Figure 1).

General socio-demographic characteristics are shown in Table 1. Participants were 73.1 (±6.6) years on average and ROC participants were older and less likely living as a couple than those from CAR.

Seroprevalence of Toxoplasma infection

Of the 1,662 individuals, 1,047 were found to be positive for anti-*T.gondii* IgG antibodies, *i.e.* a seroprevalence of 63.0% (95%CI: 60.7-65.3). The seroprevalence was lower in ROC than in CAR (p=0.002) and as a whole, lower in rural areas than urban areas (57.3% [95%CI: 53.9-60.7] vs. 68.5% [95%CI:65.4-71.6]; p<0.001) (Figure 2). In both country, the seroprevalence was significantly associated with areas (p<0.001) but the urban-rural gradient was inversed.

In bivariate analyses, *T.gondii* infection was significantly associated with increasing age in 5-year bands, country, rural areas, no education, and previous occupation. In multivariate analysis, *T.gondii* infection remained significantly associated with country, area and previous occupation (Table 2).

Median anti-*T.gondii* IgG titre was 32 (IQR 120) IU/mL (min-max: 0-15 000), 22 (105) IU/mL in ROC and 47 (128) IU/mL in CAR (p<0.001). A total of 99 participants (6.0%) had anti-*T.gondii* IgG titre>300 IU/mL, 44 (5.3%) in CAR and 55 (6.0%) in ROC (p=0.28), and 48 (2.9%) had a titre above 1000 IU/mL, 21 (2.5%) in CAR and 27 (3.2%) in ROC (p=0.40). No correlation between the anti-IgG titre and age was found (r=0.044; p=0.07).

Association between T.gondii infection and dementia

A total of 379 participants were excluded because cognitive status could not be determined for 276 of them (including 174 lost of follow up or missing) and 102 participants were diagnosed with MCI, resulting in an analytical sample size of 1,386 participants (Figure 1). Among them, 100 (7.2%) had dementia. Table 3 presents the socio-economic and clinical characteristics of participants with and without dementia. The *T.gondii* infection seroprevalence did not differ significantly based on the cognitive status: 64.0% (95%CI: 54.6-73.4) in participants with dementia *versus* 63.4% (95%CI: 60.7-66.0) in those without dementia (p=0.94). In the unadjusted and adjusted models, no association was

shown between *T.gondii* seroprevalence and dementia (respectively OR=1.0 (95%CI: 0.7-1.6) and adjusted OR=1.0 (95%CI: 0.6-1.6)).

In a sensitivity analysis, we replaced the *Toxoplasma* infection status by quintiles of anti-IgG titre (Figure 3). No association was observed in both unadjusted (p=0.13) or adjusted models (p=0.36).

DISCUSSION

To our knowledge, this large population-based study is the first study to investigate the prevalence of *T.gondii* infection in older native African adults and the first study to examine its relationship with dementia in the Central African context. We found a high prevalence of *T.gondii* infection in older people regardless of areas (urban or rural) and countries. However we did not find any association between *T.gondii* and dementia.

In African tropical countries, such as CAR and ROC, a high prevalence of toxoplasmosis is usually observed due to the low sanitary conditions, with poor or inexistent water treatment (1;2). In these conditions, soil, food and water contaminated with oocysts increase the risk of *T.gondii* infection.

The higher seroprevalence observed in CAR may be partly explained by the lower socioeconomic status in CAR compared to ROC (41). *T.gondii* infection was described as associated with poverty in different countries due to poor hygienic and sanitary conditions (42-44).

In our study, the seroprevalence was significantly higher in urban areas than in rural areas as a whole, but differences were observed at the country level. In CAR, the seroprevalence was higher in rural area than in urban area while, in ROC, an inverse rural-urban gradient was observed. In ROC, a more westernised lifestyle of Brazzaville inhabitants could lead to a more frequent meat intake than in Gamboma where meat is more expensive. Seroprevalence was also lower in people who worked or are working in farms, fisheries or with livestock. People performing better paid occupations may thus have access to a diet richer in fruits, vegetables and meat that may be contaminated with parasite. Unfortunately, soil exposure was not collected and data about food consumption were limited.

Heterogeneity in populations (women of childbearing age vs. older people) and design (case-control vs. cross-sectional survey) limits the comparison of our findings with other studies.

Surprisingly, we found a relatively large number of older adults with high antibody titres. Although studies on the evolution of the *T.gondii* serology in older populations are scarce (45), it is generally accepted that antibody titre decreases with age and are maintained at a low level over lifetime after an initial primary infection (46). Lifetime persistence of anti-*T.gondii* IgG results from continuous immune system stimulation by long-lasting tissue cysts. The usual decrease in antibody titres in older adults is hypothesized to be linked to the development of immunosenescence (47). Several hypotheses may explain the relatively high proportion of elevated titres in older people in our study: i) a primary infection during the sample collection. The detection of IgM antibodies could have confirmed this hypothesis, but it was not tested here due to financial constraints; ii) a reinfection by a different *Toxoplasma* strain that would have resulted in an increase in IgG titres. Indeed, clinical observations have shown that an immune response against a chronic infection does not prevent reinfection of immunocompetent individuals with a strain different that the one responsible for the primary infection (48). This hypothesis cannot be ruled out in our study since different genotypes have been identified in Central Africa (49-51). The immunosenescence or a T-cell exhaustion during a chronic infection (52) could facilitate the process of re-infection. iii) a non-specific and chronic immune stimulation due to different infectious agents (malaria, and other parasitic and viral diseases); iv) a genetic background leading to a higher humoral immune response in African population. Indeed, a high proportion (40.8%) of high levels of anti-*T.gondii* IgG (>400 IU/mL) was also reported in CAR in younger people (53).

Previous studies that examined the association between *T.gondii* chronic infection and Alzheimer's disease (AD) or dementia reported conflicting results (32-35). Our findings are contradictory with the ones of the only study assessing *T.gondii* infection as a correlate of dementia, carried out in a much younger population in Egypt (34). Different methodologies, including participant recruitment and statistical analyses, may explain these discrepancies. Another explanation may be the influence of the *T.gondii* strain on chronic brain infection in immunocompetent patients. In *in-vitro* cell culture systems, different immune responses or neurotransmitter expression were observed in human nervous cell infected by diverse *T.gondii* strains (54-56). In humans, a serotyping study suggested that

serological pattern consistent with Type I strain in mothers was more susceptible to be associated with psychosis in offspring (57). More recently, in a murine model of AD, only mice infected with a type II strain of *T.gondii*, a major lineage that predominates in Europe and North America, were protected against deposition of amyloid beta, a marker of AD, despite both type II and type III strains establishing a chronic CNS infection and inflammatory response (29). Mice infected with an attenuated type I strain that does not persist in mouse brain were not protected against amyloid beta deposition. Transposing data from animal models to human populations is particularly delicate as not all dementia subtypes share the same pathophysiological process and knowledge of the strains circulating in different countries is still incomplete (51;58;59). We however can reasonably think that our participants were infected by African strains, which share some genetic similarities with type I strains. Our results suggest that strains circulating in sub-Saharan Africa have no association with dementia.

The main strengths of our study are the use of a large, multicentre population-based design, the high number of participants with blood sample and a rigorous methodological method for establishing dementia diagnosis. However, a few limitations must be acknowledged. We were not able to analyse dementia sub-types, notably Alzheimer's disease, due to low frequencies. Additionally, we lack data that might influence our results such as timing of initial infection, interactions with other infectious diseases, and host genetic factors, as well as wealth or income which are potential confounders. Due to the study design, we are not able to rule out that earlier deaths due to *T.gondii* seropositivity obscured the association with dementia.

This large multicentre population-based study showed a high prevalence of *T.gondii* infection in older adults in Central Africa, with disparities in two neighbouring but different countries and areas related to socioeconomic and sanitary conditions. We failed to show any association between *T.gondii* chronic infection and dementia but future investigations should consider the association with Alzheimer's disease and Mild Cognitive Impairment. Another perspective would be to evaluate associated infectious agents as done for other neurological conditions (60).

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Declaration of interest

We declare that we have no conflict of interest.

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472 Table 1: Sociodemographic characteristics of participants based on country (n=1,662), EPIDEMCA,

473 2011-2012

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	Total	**CAR**	**ROC**	***p***
Sample, n	1662	827	835	
Age (years), n (%)				**0.010**
65-69	608 (36.6)	329 (39.8)	279 (33.4)	
70-74	427 (25.7)	216 (26.1)	211 (25.3)	
75-79	327 (19.7)	153 (18.5)	174 (20.8)	
80 +	300 (18.1)	129 (15.6)	171 (20.5)	
Sex, n (%)				0.583
Males	644 (38.8)	315 (38.1)	329 (39.4)	
Females	1018 (61.3)	512 (61.9)	506 (60.6)	
Area, n (%)				0.085
Urban	847 (51.0)	439 (53.1)	408 (48.9)	
Rural	815 (49.0)	388 (46.9)	427 (51.1)	
Education, n (%)				0.812
No education	1148 (69.2)	569 (68.9)	579 (69.4)	
At least primary school	512 (30.8)	257 (31.1)	255 (30.6)	
Missing values	*2*	*1*	*1*	
Marital status, n (%)				**0.017**
Living as a couple	616 (37.1)	283 (45.9)	333 (39.9)	
Single, widow, separated/divorced	1044 (62.9)	543 (65.7)	501 (60.1)	
Missing values	*2*	*1*	*1*	
Previous occupation, n (%)				0.790
Farmer, breeder, fisherman	817 (49.3)	409 (49.6)	408 (48.9)	
Others	842 (50.8)	416 (50.4)	426 (51.1)	
Missing values	*3*	*2*	*1*	

Table 2: Factors associated with Toxoplasma seroprevalence (n=1662), EPIDEMCA, 2011-2012

			Univariate analysis		Initial multivariate model		Final multivariate model	
	Not infected n(%)	**Infected n(%)**	**OR (95%CI)**	***p***	**OR (95%CI)**	***p***	**OR (95%CI)**	***p***
Age (years)				**0.029**		**0.003**		**0.006**
65-69	237 (38.5)	371 (35.4)	1		1		1	
70-74	174 (28.3)	253 (24.2)	0.9 (0.7-1.2)		1.0 (0.7-1.2)		0.9 (0.7-1.2)	
75-79	108 (17.6)	219 (20.9)	**1.3 (1.0-1.7)**		**1.4 (1.1-1.9)**		**1.4 (1.0-1.8)**	
80+	96 (15.6)	204 (19.5)	**1.4 (1.0-1.8)**		**1.5 (1.1-2.1)**		**1.5 (1.1-2.0)**	
Sex				0.111		0.631		
Males	223 (36.3)	421 (40.2)	1		1			
Females	392 (63.7)	626 (59.8)	0.8 (0.7-1.0)		0.9 (0.7-1.2)			
Country				**0.002**		**0.002**		**0.002**
CAR	276 (44.9)	551 (52.6)	1		1		1	
ROC	339 (55.1)	496 (47.4)	**0.7 (0.6-0.9)**		**0.7 (0.6-0.9)**		**0.7 (0.6-0.9)**	
Area				**0.001**				**0.001**
Rural	348 (56.6)	467 (44.6)	1		1		1	
Urban	267 (43.4)	580 (55.4)	**1.6 (1.3-2.0)**		**1.4 (1.1-1.8)**		**1.4 (1.2-1.8)**	
Education				**0.019**		0.288		
No education	446 (72.6)	702 (67.1)	1		1			

At least primary school	168 (27.4)	344 (32.9)	**1.3 (1.0-1.6)**		1.2 (0.9-1.5)				
Marital status				0.587					
Single, widow, separated/divorced	381 (62.1)	663 (63.4)	1		-				
Living as a couple	233 (38.0)	383 (36.6)	0.9 (0.8-1.2)		-				
Previous occupation				**<0.001**		**0.013**			**0.002**
Others	270 (44.0)	572 (54.7)	1		1		1		
Farmer, breeder, fisherman	344 (56.0)	473 (45.3)	**0.6 (0.5-0.8)**		**0.7 (0.6-0.9)**		**0.7 (0.6-0.9)**		

CAR, Central African Republic; CI, Confidence Interval; OR, Odds ratio; ROC, Republic of Congo

Table 3. Characteristics of participants according to dementia diagnosis, EPIDEMCA, 2011-2012

	No dementia (n=1286)	**Dementia (n=100)**	**p**
Age (years)			<0.001
65-69	528 (41.1)	13 (13.0)	
70-74	343 (26.7)	16 (16.0)	
75-79	226 (17.6)	20 (20.0)	
80+	189 (14.7)	51 (51.0)	
Females	713 (55.4)	80 (80.0)	<0.001
CAR	627 (48.8)	57 (57.0)	0.112
ROC	659 (51.2)	43 (43.0)	
Rural	592 (46.0)	51 (51.0)	0.337
No education	814 (63.3)	88 (88.9)	<0.001
missing data	*0*	*1*	
Living as a couple	539 (41.9)	22 (22.2)	<0.001
missing data	*0*	*1*	
Farmer, breeder, fisherman	575 (44.8)	61 (61.6)	0.001
missing data	*0*	*1*	
Cognitive score (median, IQR)	28.5 (25.4-30.4)	19.1 (15.3-21.9)	<0.001
***T.gondii* infection (positive)**	815 (63.4)	64 (64.0)	0.900
Anti-IgG titers (median, IQR)	32 (0.0-120.0)	40.5 (1.0-11.5)	0.421

CAR: Central African Republic; IQR: interquartile range

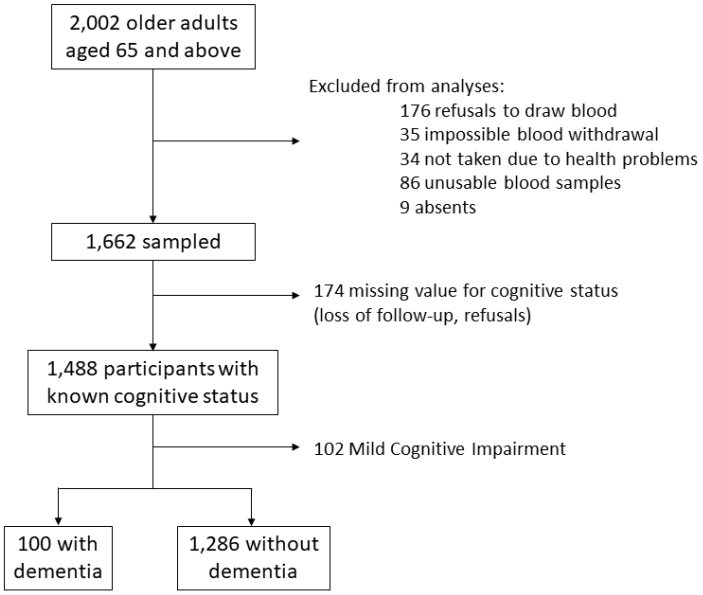
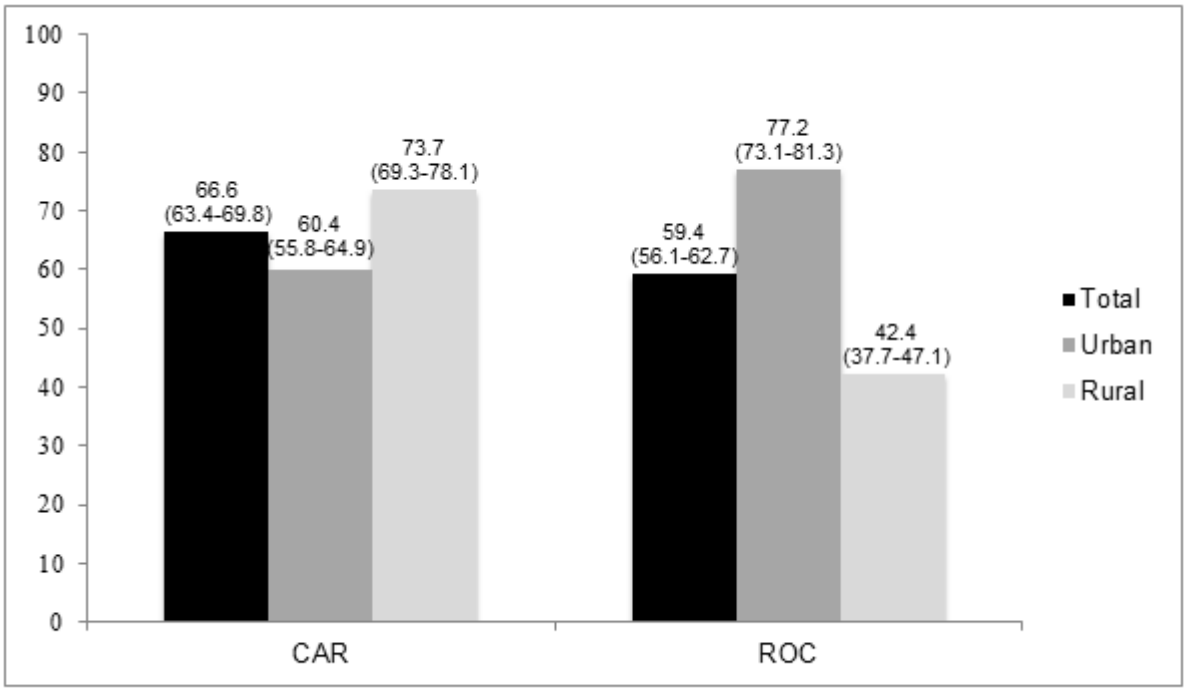


Figure 1: Flow chart of study sample, EPIDEMCA, 2011-2012



CAR Central African Republic; ROC Republic of Congo

Figure 2: Seroprevalence of *Toxoplasma* infection based on country and area, EPIDEMCA, 2011-2012.

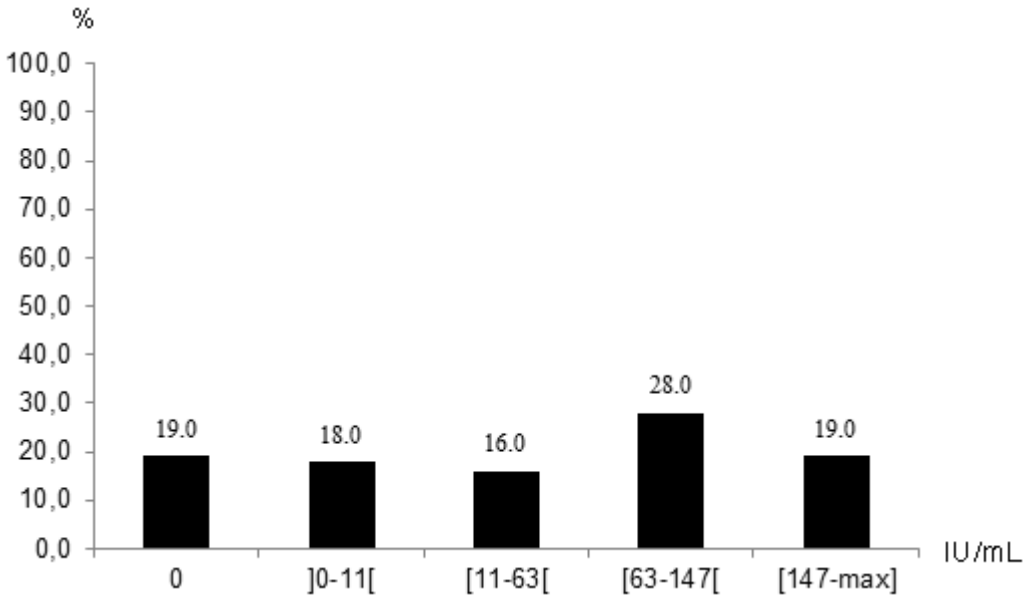


Figure 3: Prevalence of dementia based on quintiles of anti-*Toxoplasma* IgG titres (n=1,386), EPIDEMCA, 2011-2012.